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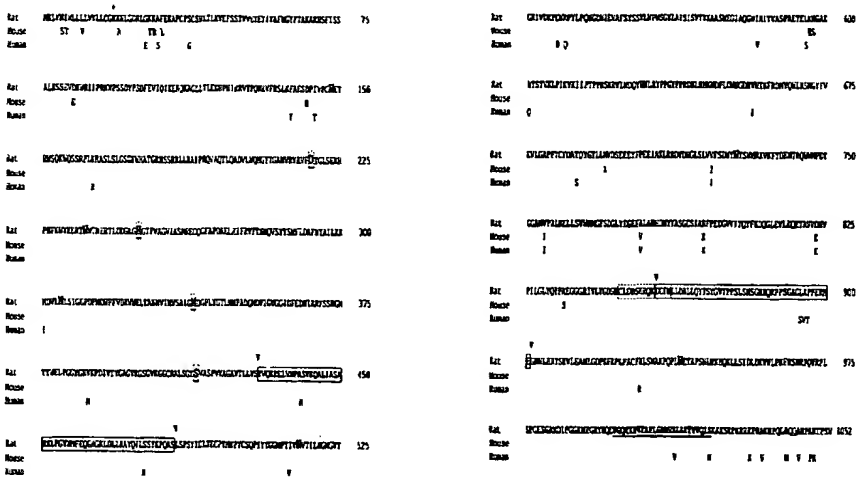

(57) Abstract

Using RT–PCR and degenerate oligonucleotides derived from the active site residues of subtilisin–kexin–like serine proteinases, we have identified a highly conserved and phylogenetically ancestral human, rat and mouse type–I membrane–bound proteinase called subtilisin–kexin–isozyme–1 (SKI–1). Computer data bank searches reveals that human SKI–1 was previously cloned but with no identified function. A SKI–1 processed fragment is secreted in culture media in a soluble form. *In vitro* studies suggest that SKI–1 is a Ca^{2+}–dependent serine proteinase exhibiting a wide pH optimum for cleavage of proBDNF. Peptides mimicking SKI–1 cleavages sites are also disclosed. SKI–1 prosegment has an *ex vivo* inhibitory effect on SKI–1 activity. The prosegment is also processed and secreted in culture media. One of its fragments is found tightly associated with the SKI–1 soluble form. Therapeutic applications for SKI–1 inhibitors are disclosed.